

CLAIMS

1. An OX40R binding agent which is the peptide sequence corresponding to amino acids 94-124 (SEQ ID NO: 6) of human OX40L.

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2. The OX40R binding agent which is a peptide sequence of human OX40L consisting of a peptide sequence corresponding to amino acids 94-124 (SEQ ID NO: 6) wherein one or more amino acids have been deleted, and comprising amino acids 107-111 (SEQ ID NO: 13) of human OX40L.

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3. The OX40R binding agent of claim 2 which is a peptide sequence of human OX40L having between 5 and 10 amino acids.

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4. The OX40R binding agent of claim 3 which is a peptide having the sequence corresponding to 107-116 (SEQ NO ID: 8), or 107-111 (SEQ ID NO: 13) of human OX40L.

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5. An OX40R binding agent which is an active mutant of peptides of claims 1 to 4, wherein one or more of the amino acids has been conservatively substituted.

6. An OX40R binding agent which is a fusion polypeptide or peptide comprising an amino acid sequence of claim 1 to 5, and an amino acid sequence belonging to a protein sequence other than human OX40L (SEQ ID NO: 1).

7. The OX40R binding agent of claim 6, wherein the fusion polypeptide or peptide comprises the amino acid sequence belonging to one or more of the following protein sequences: membrane-bound proteins, extracellular domains of membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, export signal-containing proteins.

8. An OX40R binding agent which is an active fraction, precursor, salt, or derivative of an OX40R binding agent of claims 1 to 7.

9. An OX40R binding agent which is a peptide, a peptide mimetic, or a non-peptide mimetic designed on the sequence and/or the structure of an OX40R binding agent of claim 4.

10. An OX40R binding agent which is an active conjugate or complex of an OX40R binding agent of claims 1 to 9 with a molecule chosen amongst radioactive labels, biotin, fluorescent labels, cytotoxic agents, and drug delivery agents.

11. A nucleic acid encoding for an OX40R binding agent of claims 1 to 7.

12. A vector of viral or plasmid origin which allows the expression of the OX40R binding agents encoded by the nucleic acid of claim 11.

13. A prokaryotic or eukaryotic host cell which has been transformed with an expression vector according to claim 12.

14. An isolated stable cell line substantially enriched in cells of claim 13.

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15. The cell line of claim 14 wherein the OX40R binding agent is secreted or expressed on the membrane surface.

10 16. A method of producing an OX40R binding agent of claims 1 to 7, comprising culturing cells of claims 13 to 15 and collecting said binding agent.

17. Purified preparations of the OX40R binding agents of claims 1 to 10.

18. Use of the OX40R binding agents of claims 1 to 10 as a medicament.

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19. Use of the OX40R binding agents of claims 1 to 10 as antagonists of human OX40L.

20 20. Use of the OX40R binding agents of claims 1 to 10 as antagonists of human RANTES.

21. Use of the OX40R binding agent of claims 1 to 10 as active ingredients in pharmaceutical compositions for the prophylaxis and/or treatment of autoimmune diseases, inflammations, or infections.

22. A pharmaceutical composition for the prophylaxis and/or treatment of diseases related to CD4⁺ T cells, comprising a OX40R binding agent of claims 1 to 10 as active ingredient.

23. The pharmaceutical composition of claim 22, in combination with pharmaceutically acceptable carriers, excipients, stabilizers, and/or diluents.

24. The pharmaceutical compositions of claim 22 or 23, wherein the diseases related to CD4⁺ T cells are transplant autoimmune diseases, inflammations, or infections.

25. Use of the OX40R binding agents of claims 1 to 10 or of the cells of claims 14 or 15 for the detection of the extracellular domain of OX40R protein as membrane-bound or a soluble protein.

26. Use of the OX40R binding agents of claims 1 to 10 or of the cells of claims 14 or 15 for the detection of activated CD4⁺ T cells.

27. Supports for the detection, the purification, and / or the concentration of OX40R extracellular domain, as a membrane-bound or a soluble protein, or of activated CD4⁺ T cells, said supports having an OX40R binding agent of claims 1 to 7 in an immobilized form.

28. Methods for the detection, the purification, and / or the concentration of OX40R extracellular domain, as membrane-bound or a soluble protein, or of activated CD4⁺ T cells in a sample, said method comprising contacting said sample with the supports of claim 27 or with the cells of claims 14 or 15.

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29. A method of claim 28, wherein the method is used to diagnose a condition associated to decreased or increased presence of CD4⁺ T cells or of soluble OX40R protein.

10 30. Methods for the prophylaxis and/or treatment of autoimmune diseases, inflammations, or infections comprising the administration of an OX40R binding agent of claims 1 to 10 or of the cells of claims 14 or 15.

15 31. A screening assay for the determination of the nature and the activity of compounds modulating OX40R-OX40L interactions comprising:

a) Forming a sample comprising the following elements:

- i. An element constituting the OX40R binding agent, chosen amongst the compounds of claims 1 to 10, the cells of claims 14 or 15, and the supports of claim 27;
- 20 ii. An element constituting the OX40R moiety, chosen amongst a protein comprising the extracellular domain of OX40R, a cell line expressing OX40R extracellular domain on its surface, and a cell line secreting extracellular domain of OX40R; and

iii. The compound(s) to be tested as modulator(s) OX40R-OX40L interactions.

b) Detecting, directly or indirectly, the effect of the compounds (iii) on the interactions between the elements (i) and (ii);

5 c) Comparing the effect detected in (b) amongst samples different in terms of quality and / or quantity of the elements of (a).

32. A kit for detecting extracellular domain of OX40R protein or activated CD4⁺ T-cells which comprises an OX40R binding agent according of claims 1 to 10, a cell
10 of claims 14 or 15, or a support of claim 27.

33. A kit of claim 32 for the diagnosis of a condition due to a decreased or increased presence of CD4⁺ T cells or of soluble OX40R protein in a sample obtained from a patient.

15 34. A kit for screening compounds inhibiting the interaction of a protein ligand with a membrane-associated protein, comprising the extracellular portion of the membrane-associated protein and the protein ligand as fusion proteins having different tag sequences.

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